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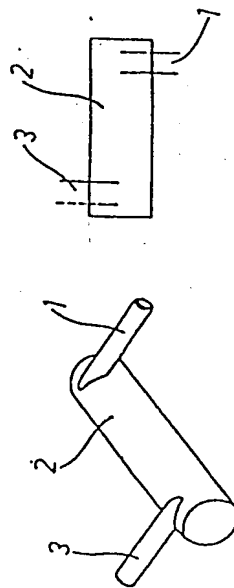


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(57) Abstract

A device for a more effective pulverization of particles and/or agglomerates of a powdered inhalation medicament, comprising a chamber (2) intended for medicament and substantially closed at one end thereof, said chamber being provided with at least one air inlet port and a powdered medicament outlet port. The chamber (2) substantially closed at one end said, chamber being rotationally symmetrical in shape or its cross-section perpendicular to the centre axis thereof being substantially circular in shape and without substantial flow obstacles. The inlet and outlet ports are spaced from each other in the direction of the centre axis of chamber (2). Said inlet port (1) being designed to direct the air inflow into the vortex chamber substantially parallel to the tangent of said chamber.

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# Device for more effective pulverization of a powdered inhalation medicament

The present invention relates to a device which is based on centrifugal force for achieving more effective pulverization of a powdered inhalation medicament in a manner that the penetration of medicament into the lungs is improved and the adhesion to the upper respiratory passages is reduced for alleviating the side effects caused thereby.

It is generally known that the size of medicament particles should be 1-5 microns, preferably 2-3 microns, for the best possible penetration into their destination, i.e. deep into the lungs. The most common metering device is a so-called inhalation aerosol which is quite readily capable of reaching the optimal particle size. In addition to inhalation aerosols, an increasing number of powder inhalators are presently in use as these offer certain benefits, e.g. there is no need for ozone-destroying propellants. Several clinical studies have indicated that, with the same amount of medicament, the powder inhalators do not achieve the same effect as

inhalation aerosols but it takes up to 2-3 times larger dosages to get the same results. The reason for this is considered to be the fact that a powdered medicament issuing from powder inhalators has too large a particle size. Thus, most of the medicine dosage coming out of inhalators is retained in upper respiratory passages which, with certain medicines, can cause serious side effects. The medicine dosages required for different inhalation medicaments vary considerably, the smallest being appr. 0.01 mg and the largest 20 mg. When small amounts of medicine are metered in powdered form, it is generally necessary to use some adjuvant or carrier, so

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that the sufficiently precise measuring of a dosage would be possible with the present technology. No matter if the dosage comprises just medicine or has a carrier admixed therein, the medicine dosage substantially comprises inter-adhered particles and most of these agglomerates are too large to penetrate into the lungs. As the agglomerates are released in a powder inhalator into an air flow passing into the lungs of a patient, there will occur some dispersal of these particle deposits, said dispersal resulting from the formation of a powdered medicament and the construction of an inhalator. It is known that constructions creating a strong turbulence are capable of more effective pulverization.

In practice, however, no prior known powder inhalator structure and/or medicine formulation has produced results that would be equal to those achieved by an ordinary inhalation aerosol. It has been suggested as a partial solution that inhalation should be effected with as much force as possible, whereby the turbulence and pulverization of particles would accordingly be most effective. However, a quick inhalation is difficult for a person suffering e.g. from serious asthma and, on the other hand, a quick inhalation increases the residue in upper respiratory tracts. According to studies, pulverization of agglomerates is indeed intensified but the overall benefit is marginal. The best pulmonary penetration in relation to the adherence of medicament to upper respiratory tracts has been achieved by slow inhalation, corresponding to a flow rate of appr. 30 l/min or 0,5 l/sec.

The only prior known powder inhalator is the device described in Finnish Patent application No. 871000 which has been designed in an effort to produce a clearly de-

fined turbulence for pulverizing agglomerations of medicine. The centrally directed deflectors inside the device or the helical chute are explained to set the air flow in a spinning motion, whereby the medicine particles entrapped in the air abrade as a result of centrifugal force against the walls of the structure as well as collide into each other with resulting pulverization.

The device described in the cited application has been marketed under a trademark Turbuhaler<sup>®</sup> (Draco, Sweden) and the pulverizing structure therein is a helical chute or groove. Laboratory tests indicated that this device had a relatively good pulverization of agglomerates of medicine which could be very distinctively intonified, however, by means of a device of the present invention. In view of the pulverization of agglomerates or accumulations of medicine, there are a few defects in the device. The helical groove has in the centre thereof an open space having less air resistance than inside the groove. Accordingly, the flow rate of air and centrifugal force on the circumference of the groove are less than theoretical. Since the particles advance in the groove under a force caused by air resistance and centrifugal force tends to push the particles perpendicularly to the circumferential tangent, the actual force applied to the particles is a resultant of these forces and is applied diagonally relative to the circumferential tangent. Thus, the centrifugal force resulting from the spinning motion cannot be utilized in full extent for the pulverization of accumulations. In all deflector structures according to the cited application, the particles escape from the device within a few thousandths of a second when using conventional inhalation rates of 30-60 l/min and that is a very short time for an effective pulverization. The residence time can be lengthened e.g. by increasing the number of helices

in groove portions or the number of separate deflector structures or the length of zigzagging air flow channels, but this would complicate manufacturing and cleaning and medicine residues in the actual device would increase. After all, cleaning of the structures disclosed in the cited application is difficult as it is.

The European Patent application No. 215559 discloses a powder inhalator, wherein one or more balls travel as a result of air flow around a periphery which is substantially circular in configuration. The air flow comes into contact with the periphery tangentially relative thereto. The medicine is adhered either to the surface of balls or to the surface of the circulation periphery from which it is removed and is pulverized by the action of the rolling balls. The device employs a centrifugal force for fractionating loose particles in a manner that the discharge of air occurs centrally relative to the circulating path. Thus, the pulverization of medicine is a result of a mechanical contact between the balls and the surface.

In the cited structure, the balls close the circulating path for the most part and, thus, there cannot be high speeds of circulation for the balls or medicine particles and, hence, there cannot be major centrifugal forces. It is obviously difficult to use the device for repeatedly metering out exact doses of medicine.

The British Patent No. 1485163 describes a device, wherein a powdered medicament containing elongated capsule provided with pierced ends is set through the action of inhalation air in a rotating motion inside a cylindrical mixing chamber. Piercing of the capsule is effected in a capsule-shaped space which is in open

communication with the mixing chamber and the capsule is jerked therefrom along with the air flow into the mixing chamber to spin around its vertical axis. The medicament flings through the ends of the capsule into the mixing chamber and further into an inhalation channel. The device according to this Patent has been marketed under the tradename Inalatore I.S.F. Laboratory tests showed that the device had a reasonable pulverizing effect for accumulations of medicine but a distinctly poorer effect than what is achieved by a device of the present invention.

The device disclosed in the cited Patent would have an improved pulverizing effect if the rotating speed of a capsule and air in the mixing chamber could be increased for using the centrifugal force more effectively for pulverization. This is impossible with the cited structure since it is prevented by the own mass of a capsule and by the friction resulting from its rotation. In addition, the space in communication with the mixing chamber and intended for piercing the capsule is asymmetrical relative to rotating direction and produces a decelerating turbulence.

The British Patent No. 1331216 of the same Patent Owner discloses a device operating on the capsule discharging mechanism, wherein the capsule after piercing is carried into a cylindrical mixing chamber by the action of inhalation. The air arrives in this chamber through a plurality of tubes directed tangentially to the circulation periphery setting the capsule in a rotating motion and transferring the medicine from the capsule into the inhalation air. This structure is also not capable of producing sufficient centrifugal forces for the pulverization of accumulations of medicine because of the

capsule's mass, rotational friction and air resistance.

The British Patent No. 1472650 discloses a device for the inhalation of a powdered medicament contained in a capsule. The capsule is purged in a manner that some of the inhalation air is passed through a pierced capsule while most of the air travels past the capsule.

However, piercing of the capsule is effected centrally towards the longitudinal axis of the capsule and there is no purpose to create inside the capsule a turbulent flow that would produce a major centrifugal force.

Also, according to laboratory tests, the device set forth in the cited patent (Boehringer Ingelheim) did not produce a powerful turbulence inside the capsule. Also the pulverizing effect of the device for accumulations of medicine was conventional.

The British Patent No. 1118341 describes a structure for purging an open, medicine-containing container into inhalation air. As one alternative to sucking the air into a chamber containing a medicine container there is shown a structure which uses deflectors for setting the air flow in a spinning motion in the chamber. The cited Patent specification discloses that an object is rather to create irregular turbulence and passage of air flows against the deflectors than to set the air in a rotating motion as rapid as possible. Thus, the internal positioning of deflectors in the chamber severely restricts the rotating motion but creates effectively other turbulence.

Prior known are also several structures, wherein a medicament-containing capsule is pierced prior to dosage, set in its holder in a rotating motion by means of inhalation air or cut open. Prior known are also

structures, wherein a medicament is transferred from a capsule into inhalation air by the application of pressurized air. Furthermore, there are known structures, wherein a powdered medicament is transferred for inhalation from a disc or a separate powdered medicament container carrying several doses of medicine.

US 4046146, 4116195, 4117844, 4210140

GB 1182779, 1396258, 1404338, 1457352, 1459426, 1502150, 1521000

Finnish Patent publication 76258, Finnish application 863094 and 883767, Danish publication print 153631 B.

None of the above cited and examined publications discloses a structure, wherein a powdered medicament would be pulverized by means of inhalation or an external gas pressure by the application of a centrifugal force resulting primarily from a powerful rotating motion with a structure described hereinafter.

In a device of the invention, a powdered medicament intended for inhalation is pulverized on the basis of a sufficiently powerful centrifugal force prior to or during inhalation. The centrifugal force is produced through the action of inhalation or the flow of an external pressurized gas. In a device of the invention, a powdered medicament is entrapped in a gas flow and forced in a substantially circular or rotationally symmetrical space to such a powerful rotating motion that an effective splitting of accumulations of medicine is obtained. This is effected in a rotationally symmetrical chamber whose largest internal diameter can be 30 mm. With a device of the invention, the pulverization time of large, hard-splitting particles can be increased and, as the rotating motion is over, the major particles, e.g. the carrier, can be mostly retained in



the chamber to prevent its passage into the respiratory tracts of a patient. A device of the invention is distinctly more effective than the prior known solutions, and thus, as well as by virtue of the ability of retaining large particles, it is possible to improve the effect of medication and to reduce the side effects caused by a medicament remaining in the upper respiratory tracts.

Upon the application of this device to inhalation conducted by a patient, it should be appreciated that the best penetration of medicine particles into the lungs is obtained by means of a slow inhalation with a duration of appr. 5 seconds. Thus, the inhalation rate will be 20-30 l/min. In order to facilitate such trouble-free operation e.g. for a person with a difficult asthma, the inhalation resistance caused by the device itself may not be too high. However, all deviations from a laminar air flow add to the inhalation resistance in powder inhalators no matter how effectively such deviation or turbulence pulverizes accumulations of medicine. Because, however, the inhaling power of a patient sets a practical limit to the force that can be used in an inhalator for the pulverization of accumulations of medicine, the optimal exploitation of this force is of major importance in view of the proper operation of the device. When developing this device, various turbulences and collision patterns of particles were compared with centrifugal force and that latter was found overwhelmingly superior.

If a cylinder with one solid end is supplied with an air flow tangentially from the side at its solid end, such flow is first set in a rotating motion dictated by its entrance speed which produces a centrifugal force. Magnitude of this force can be calculated from the

formula:

$$a = \frac{v^2}{r} \quad \text{wherein } a = \text{acceleration}$$

$$v = \text{air flow rate}$$

$$r = \text{radius of cylinder}$$

When gravity acts on a mass at an acceleration of  $9,91 \text{ m/s}^2$ , the  $a: 9,91 \text{ m/s}^2$  indicates the number of times the mass (weight) of a particle circulating along the inner wall of a cylinder entrapped in an air flow is multiplied as a result of the centrifugal force.

If in such a well-operating device (fig. 1) the radius of an inlet tube is 3 mm and the radius of a vortex cylinder is 6 mm, the suction rate of 30 l/min corresponding to a slow inhalation provides a maximal air circulation rate of  $17,68 \text{ m/s}$  in the cylinder and an acceleration of  $52,1 \times 10^3 \text{ m/s}^2$ , the latter being 5310 times the acceleration of gravity. According to this, the weight of medicine particles would be multiplied by more than 5000, which fully expels the power of the device. When measuring the negative pressure caused by inhalation at a suction rate of  $0,5 \text{ l/s}$ , the discovered reading was -15 mbar but when inhaling in the reverse direction, the reading was just -4,5 mbar. The difference reflects the energy required for the generation of a centrifugal force since, when inhaling in the reverse direction, there will be no turbulent flow and air resistance is quite close to that of a laminar flow. Tests on patients have revealed that the inhalation resistance should not exceed the reading corresponding to a negative pressure of 15-20 mbar. On the other hand, a suitable inhalation resistance can be used to prevent too fast an inhalation as the latter would in-

crease the medicine residue in upper respiratory tracts. Hence, in a device of the invention it is possible to set an inhalation resistance particularly by adjusting the diameter of an inlet tube and that of the cylinder while the force of inhalation can still be effectively used for the pulverization of accumulations of medicine. If the centrifugal force is produced by the application of a pressurized gas, e.g. compressed air, the physiology of a patient no longer controls the power of the device. Thus, the diameter of cylinder and inlet tube can be reduced. In a device in which the inlet tube had a diameter of 1 mm and the cylinder had a diameter of 4 mm, the 1/2 bar overpressurized air had a measured air flow rate through the device of 4,5 l/min. Thus, the air flow rate in the inlet tube and on the periphery of the cylinder was 95,5 m/s which, in accordance with the above-described formula, provides 465 000 times the gravitational acceleration when the speed of rotation is 7600 r/s. In this context, it should be appreciated that the circulating speed of particles is considerably slower than the calculated readings as a result of e.g. air resistance and abrasive friction, but the calculations provide an impression of the magnitude of those forces involved in the operation of the device. An instantaneous positive pressure of appr. 1 bar can even be reached with a manually operated pump and higher pressures can be obtained by using e.g. a manually or electrically rechargeable pressure container.

Because of the operating principle of the device, the cylinder cannot be allowed to contain any structures substantially impeding free air circulation, such as deflectors, grooves or capsules or parts thereof spinning along with the air flow, with the exception of carriers containing medicine particles or a formulation. Even

the relatively large amounts of carriers contained in certain medical formulations clearly hamper and decrease the speed of rotation. The cylinder must have a cross-section which is substantially circular in every part thereof. However, this makes it possible that the cylinder can have a cross-section which is e.g. conical or asymmetrically multiformed for using a centrifugal force for the fractionation of particles by the application of generally known centrifugating principles. A rotationally symmetrical axle or a part thereof extending in the same direction as the longitudinal axis of a vortex chamber does not disturb the action.

The following are examples of devices of the invention. Fig. 1 shows a cylindrical device having a cross-section which is in all aspects in the form of an equiradius circle. Fig. 2 shows a cylinder which is solid at both ends and both the entrance and exit of air occur tangentially. In fig. 3 the cylinder has a conical cross-section and in fig. 4 a quadratic cross-section, the discharge being effected centrally through the gable of the cylinder. In these structures, during a circulating motion, there occurs fractionation of particles in a manner that larger particles tend to circulate continuously on the largest periphery of the cylinder and shall not be able to escape through the central outlet port until pulverized to sufficient fineness.

It has been found out experimentally that the pulverization time of large particles can be further increased if the structure of fig. 3 or 4 is alongside the inlet tube provided with a solid chamber extension. At the end of air flow, the non-pulverized particles are mostly retained in this space and cannot work their way into the pharynx of a patient. Fig. 5 shows a more detailed

structural drawing of such a vortex chamber. The medicine agglomerates arrive along with an air flow from a tube 1 into a chamber provided with a constriction 2 for preventing the immediate departure of large particles from the chamber under the action of a centrifugal force. The large particles are able to rotate and spin in a closed chamber section 3 and, after a sufficient pulverization, are able to escape into an inhalation tube 4. The closed chamber section comprises a removable plug 5 for facilitating the cleaning of the chamber. The optimum diameter of a vortex chamber operating by the action of inhalation is 10-20 mm. The pulverization effect is excellent and the substantially tangential setting of an inlet tube is possible as long as the air resistance remains reasonable. If the diameter is increased, the pulverization effect deteriorates in a manner that, with a diameter of more than 30 mm, the pulverization effect is no longer significant.

It should be noted that also a conventional powdered medicament capsule can be used as a vortex chamber with suitable provisions. Fig. 6a, b and c illustrates an example of such a device whose operation is based on an air flow produced by inhalation. Fig. a shows a section in the axial direction of a capsule on plane A and figs. b and c show sections perpendicularly to the preceding one on planes B and C. A medicine capsule 8 is placed in a cylindrical space 7. Therefore, the device is hinged at 16 and opens along a line 9. A latch (not shown in the figures) indicated at 10 locks the parts to each other so as to immobilize the capsule by tightening at 11. The capsule is pierced by means of a dowel device 12 at both ends thereof in a manner that the air inflow through a tube 13 is tangentially direct-

ed into a hole 14. Most of the air flows past hole 14 into a space 15 provided at a hole 17 with a constriction producing a Venturi effect. Thus, there is a positive pressure at hole 14 and a negative pressure at hole 17 which intensifies the creation of a turbulent flow inside the capsule. The device can be connected to vortex chambers as shown in figs. 1-5 for obtaining a complete powder inhalator fitted with a dual vortex chamber.

When operating a device as shown in fig. 6 by the action of inhalation, said holes 14 and 17 must be sufficiently large for producing a sufficient turbulence inside the capsule. This requires that the capsule be made of some tough material for preventing fractures when piercing the holes. Also the size and shape of a capsule are significant factors. A capsule with flat ends serves the purpose better than a traditional round-headed capsule.

It is obvious that with a more intense air flow the pulverization effect of a device as shown in fig. 6 can be improved. This can be achieved e.g. by using a hand puppet to pass a small amount of pressurized air into hole 17. In that case, inhalation must be effected simultaneously with the pressing of a puppet unless some structures are used for retaining the pulverized particles for subsequent inhalation.

The devices shown in figs. 1-5 can be connected to all available powder inhalators. In fig. 7, a device as shown in fig. 5 is connected to a powder inhalator (Turbuhaler<sup>R</sup>, Draco, Sweden) described in Finnish Patent application No. 871000 in a manner that the device replaces the helical groove included in Turbuhaler<sup>R</sup>.

In fig. 8, a version of the device shown in fig. 2 fitted with two outlet tubes is connected to a powder inhalator described in Finnish Patent application No. 883767, wherein a medicine capsule is emptied by means of compressed air produced with a hand pump. In this type of combination, the inhalation must be effected at the same time as the pump is pressed. Inhalation air is picked up from the area alongside the vortex chamber outlet tubes.

The operating ability of a device of the invention is highly dependent on the properties of a presently used medicament and possible additives. In order to achieve the best possible result, different medical formulations require the use of different vortex chamber designs. The manufacturing material of a vortex chamber must also be selected in a manner that the adherence of a medicament to the chamber is as insignificant as possible and that the chamber has an inner surface which withstands major abrasive forces without excessive wear.

The power of a device of the invention has been studied by the application of a method generally used in this field, wherein the inhalation effected by a patient is simulated to suck a powdered medicament into a particle separator (a cascade impactor). This is to find out the number and mean particle size of those medicine particles that are capable of passing into their pulmonary site of action (less than 5,8 microns):

The following table illustrates results of the outputs of a device of the invention as well as prior known powder inhalators included as a reference.

Powdered medicine	Inhalator	% of particles less than 5,8 microns of a dosage	Mean particle size (micron)	Patent reference to inhalator
1.1 Ventoline 0,2 mg Rotacaps	Rotahaler <sup>R</sup>	22,7	7,6	Danish publ. No. 153631 B
1.2 Ventoline 0,2 mg Rotacaps	Inalatore I.S.F.	30,3	5,8	GB 1485163
1.3 Ventodisks 0,2 mg	Diskhaler <sup>R</sup>	26,0	5,8	Finnish Pat.appl. No. 863094
1.4 Ventoline 0,2 mg Rotacaps	Fig. 5 Prototype	61,6	2,4	
2.1 Lomudal 20 mg caps.	Spinnhaler <sup>R</sup>	14,0	9	GB 1182779
2.2 Lomudal 20 mg caps.	Fig. 5 Prototype	38,2	2,3	
3.1 Bricanyl 0,5 mg	Turbyhaler <sup>R</sup>	35,5	4,1	Finnish Pat.appl. No. 871000
3.2 Bricanyl 0,5 mg	Fig. 4 Prototype	58,3	2,4	

In order to obtain comparable results, all reference groups employed the same pharmaceutical formulations:

- 1.1 - 1.4 salbutamol as pharmaceutical, lactose as carrier (Glaxo, GB)
- 2.1 - 2.2 Na-Chromokligate as pharmaceutical, no carrier (Zions, GB)
- 3.1 - 3.2 terbutaline as pharmaceutical, no carrier (Draco, S)

In prototypes of the invention, the dosage of a powdered medicine was effected by means of the metering unit of a powder inhalator according to US Patent 4046146 which, if used by itself, does not have a distinct particles pulverizing effect as the same results were obtained by a manual powder feeding. Other inhalators included in the comparison are commercially available. The results take into consideration also the medicament stuck in the metering unit and inhalators.

When assessing the results, an objective of powder inhalators should also be considered: to administer as much as possible of a medicine dose into the inhalation of a patient as particles whose size is 1-5 microns, preferably 2-3 microns, for the most likely pulmonary penetration.

In all reference groups, a prototype of the invention was overwhelmingly the best. The number of pharmaceutical particles of the proper size category was 1,6 - 2,7 times more than that of reference particles and the particles had exactly the optimum mean size.

Thus, a device of the invention is capable of considerably improving the penetration of a medicine into the lungs and, thus, to reduce the residue in upper respira-

tory tracts for alleviating the side effects caused thereby. The present structures are readily cleanable e.g. with a small brush. The structures can be readily manufactured e.g. as pressure casting of plastics. A device of the invention can be connected to all prior known powder inhalators. It can be used both with separate medicine capsules and in association with a powder container containing a plurality of doses. The device operates both through the action of inhalation and a pressurized gas, e.g. air.

Claims

1. A device for a more effective pulverization of particles and/or agglomerates of a powdered inhalation medicament, comprising a chamber (2) intended for medicament and substantially closed at one end thereof, said chamber being provided with at least one air inlet port and a powdered medicament outlet port, characterised in that the chamber is a vortex chamber (2) substantially closed at one end thereof, said chamber being rotationally symmetrical in shape or its cross-section perpendicular to the centre axis thereof being substantially circular in shape and without substantial flow obstacles, said inlet and outlet ports being spaced from each other in the direction of the centre axis of chamber (2) and said inlet port (1) directing the air inflow substantially parallel to the tangents into the vortex chamber.

2. A device as set forth in claim 1, characterised in that said inlet port (1) is located in the chamber wall adjacent to the closed end of the vortex chamber.

3. A device as set forth in claim 1, characterised in that said inlet port (1) is closed at both ends thereof.

4. A device as set forth in any of claims 1-3, characterised in that the diameter of vortex chamber (2) varies in a stepless and/or stepwise fashion.

5. A device as set forth in any of claims 1-4, characterised in that between vortex chamber (2) and outlet port (3) is fitted a constriction (6) for retaining

ing major particles.

6. A device as set forth in claim 1, 2 or 4, characterised in that the closed end of vortex chamber (2) is a rotationally symmetrical space (4) which consists of a removable plug (5).

7. A device as set forth in any of claims 1-6, characterised in that the device is connected to a per se known inhalation device.

## AMENDED CLAIMS

[received by the International Bureau on 14 November 1990 (14.11.90); original claims 1, 2 and 5 amended; other claims unchanged (2 pages)]

1. A device for a more effective pulverization of agglomerates in a single-dose of a powdered inhalation medicament, comprising a chamber (2) intended for medicament and substantially closed at one end thereof, said chamber being provided with at least one air inlet and an outlet for directing the air and the medicament particles contained therein into the airways of the user of the device, characterized in that the chamber is a vortex chamber (2) substantially closed at one end thereof, said chamber being rotationally symmetrical in shape or its cross-section perpendicular to the centre axis thereof being substantially circular in shape and without substantial flow obstacles, said inlet and outlet being spaced from each other in the direction of the centre axis of chamber (2) and said inlet (1) directing the air inflow substantially parallel to the tangents into the vortex chamber.

2. A device as set forth in claim 1, characterized in that said inlet (1) is located in the chamber wall adjacent to the closed end of the vortex chamber.

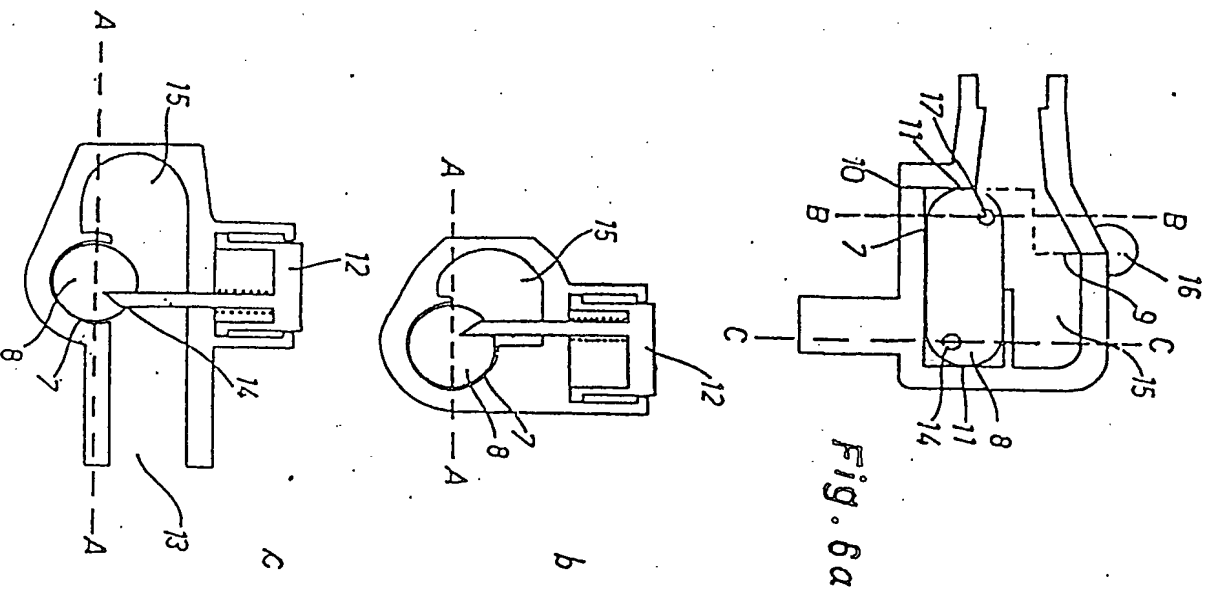
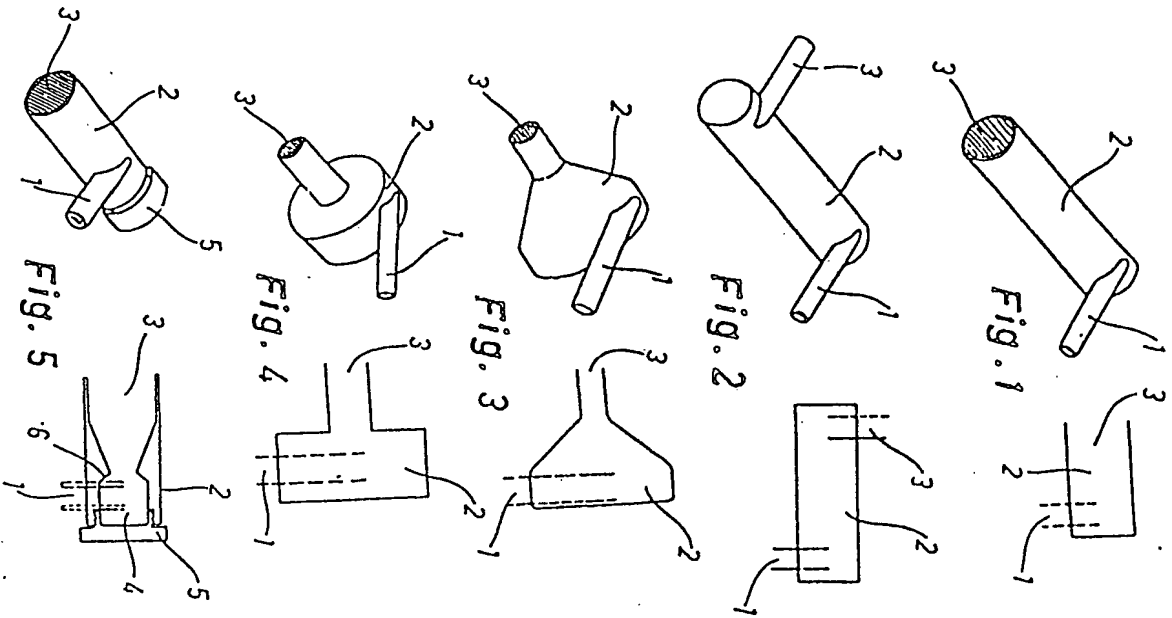
3. A device as set forth in claim 1, characterized in that said vortex chamber (2) is closed at both ends thereof.

4. A device as set forth in any of claims 1-3, characterized in that the diameter of vortex chamber (2) varies in a stepless and/or stepwise fashion.

5. A device as set forth in any of claims 1-4, characterized in that between vortex chamber (2) and outlet (3) is fitted a constriction (6) for retaining major particles.

6. A device as set forth in claim 1, 2 or 4, characterized in that the closed end of vortex chamber (2) is a rotationally symmetrical space (4) which consists of a removable plug (5).

7. A device as set forth in any of claims 1-6, characterized in that the device is connected to a per se known inhalation device.





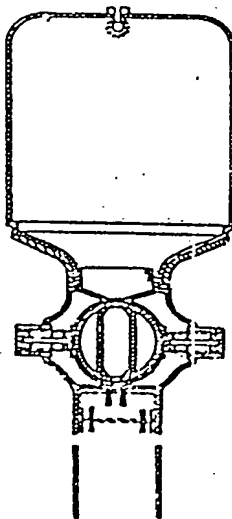


Fig. 8

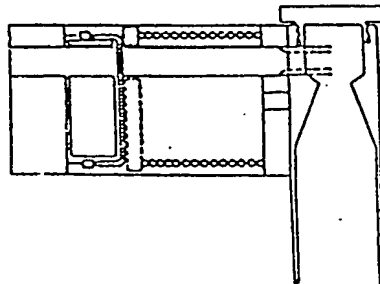


Fig. 7

INTERNATIONAL SEARCH REPORT		International Application No. PCT/FI 90/00159	
I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all) According to International Patent Classification (IPC) or to both National Classification and IPC IPC5: A 61 M 15/00			
II. FIELDS SEARCHED Minimum Documentation Searched Classification System Classification Symbols			
IPC5 A 61 M			
Documentation Searched other than Minimum Documentation in the extent that such documents are included in Fields Searched			
SE, DK, FI, NO classes as above			
III. DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of Document <sup>(1)</sup> with indication, where appropriate, of the relevant passages <sup>(2)</sup>	Excerpt in Claim No. 13	
X	EP, A1, 0005585 (FISONS LIMITED) → 81 28 November 1979, see figures 1, 2	1, 5-7	
X	FI, B, 71488 (FISONS LIMITED) 10 October 1986, see figure 5; claim 1	1-2, 4-7	
X	DE, B2, 2449179 (I.S.F.S.P.A.) 3 July 1980, see figures 1, 2 - 05.3.11.7	1-2, 4-7	
X	FR, A, 1445520 (M. HAMILTON O. HAZEL) 6 June 1966, see figures 1, 2	1-3, 6-7	
A	SE, B, 453566 (AB DRACO) 15 February 1988, see the whole document	1-2, 4, 6-7	
* Special categories of cited documents: 18 * A* document filed after the international filing date which is not considered to be a particular art reference * E* earlier document but published on or after the international filing date * L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another document or other special reason (as specified) * O* document referring to an oral disclosure, use, exhibition or other means * P* document published prior to the international filing date but not containing the priority date claimed			
* T* later document published after the international filing date which is not considered to be a particular art reference but which is cited to substantiate the principle or theory underlying the invention * X* document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step * Y* document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step, such combination being obvious to a person skilled in the art * Z* document member of the same patent family			
IV. CERTIFICATION			
Date of the Actual Completion of the International Search		Date of Mailing of this International Search Report	
21st September 1990		1990 -09- 25	
International Searching Authority		Signature of Authorizing Officer	
SWEDISH PATENT OFFICE		Leif Karnsäter <i>led Karnsäter</i>	

III. DOCUMENTS CITED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category	Class of Document, with indication, where appropriate, of the relevant passages	Reference to Class No.
A	EP, A1, 0215559 (HAKA WILHELM ET AL) 25 March 1987, see the whole document	1-2,7

ANNEX TO THE INTERNATIONAL SEARCH REPORT  
ON INTERNATIONAL PATENT APPLICATION NO. PCT/FR 90/00159

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the Searcher's Patent Office (IPO) file. The Searcher's Patent Office is to be very helpful for those participants which are directly given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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